

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference SUVN-RK-002	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/IN 03/00209	International filing date (day/month/year) 05/06/2003	(Earliest) Priority Date (day/month/year) 28/11/2002
Applicant SUVEN PHARMACEUTICALS LTD.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 11 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.



the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing:



contained in the international application in written form.



filed together with the international application in computer readable form.



furnished subsequently to this Authority in written form.



furnished subsequently to this Authority in computer readable form.



the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.



the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2.



Certain claims were found unsearchable (See Box I).

3.



Unity of invention is lacking (see Box II).

4. With regard to the **title**,



the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

**N-ARYLSULFONYL-3-SUBSTITUTED INDOLES HAVING SEROTONIN RECEPTOR AFFINITY,
PROCESS FOR THEIR PREPARATION AND PHARMACEUTICAL COMPOSITION CONTAINING THEM**

5. With regard to the **abstract**,



the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.



as suggested by the applicant.



because the applicant failed to suggest a figure.



because this figure better characterizes the invention.



None of the figures.

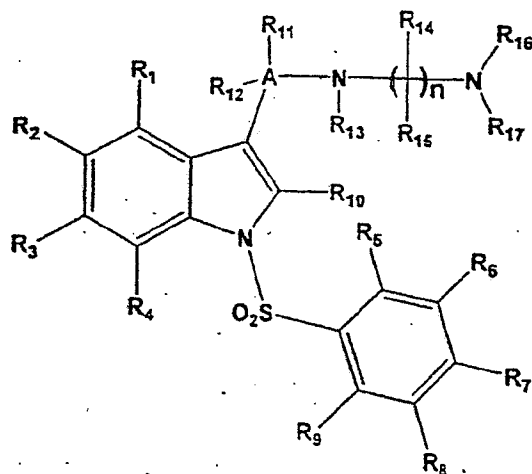
INTERNATIONAL SEARCH REPORT

International application No.

PCT/ IN 03/ 00209

Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

The present invention relates to novel N-arylsulfonyl-3-substituted indole compounds, their derivatives, their analogs, their tautomeric forms, their stereoisomers, their geometric forms, their N-oxides, their polymorphs, their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates and pharmaceutically acceptable compositions containing them. This invention particularly relates to novel N-arylsulfonyl-3-substituted indoles of the general formula (I), their derivatives, their analogs, their tautomeric forms, their stereoisomers, their polymorphs, their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates, and pharmaceutically acceptable compositions containing them. This invention also relates to the process for preparing compounds of the general formula (I), pharmaceutical compositions containing such compounds and the use of such compounds and compositions in medicine. This invention also relates to the novel intermediates involved therein and process of their preparation.



General Formula (I)

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D209/14 C07D209/18 C07D401/12 C07D403/06 C07D209/12
A61K31/4045 A61P25/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, PAJ, CHEM ABS Data, BEILSTEIN Data, WPI Data, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 02 058702 A (SMITHKLINE BEECHAM CORP ;DHANAK DASHYANT (US); KNIGHT STEVEN D (US) 1 August 2002 (2002-08-01) page 3, line 10 -page 4, line 2; examples 13,18 ---	1,3-5, 14,20-26
X	WO 02 47687 A (SMITHKLINE BEECHAM CORP ;DHANAK DASHYANT (US); KNIGHT STEVEN D (US) 20 June 2002 (2002-06-20) page 3, line 6 -page 3, line 25; example 1 ---	1,3-5, 14,20-26
X	PATENT ABSTRACTS OF JAPAN vol. 2000, no. 15, 6 April 2001 (2001-04-06) & JP 2000 344744 A (SS PHARMACEUT CO LTD), 12 December 2000 (2000-12-12) Formula (I) abstract --- -/--	1,3-5, 14,20-26

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *Z* document member of the same patent family

Date of the actual completion of the international search

10 September 2003

Date of mailing of the international search report

24/09/2003

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
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Authorized officer

Usueli, A

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LE BORGNE M ET AL: "New selective nonsteroidal aromatase inhibitors: synthesis and inhibitory activity of 2, 3 or 5-(alpha-azolylbenzyl)-1H-indoles" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, OXFORD, GB, vol. 9, no. 3, 8 February 1999 (1999-02-08), pages 333-336, XP004157224 ISSN: 0960-894X Scheme II, compound 21 ---	1,3-5, 14,20-26
X	J. HETROCYCLIC CHEM., vol. 29, 1992, pages 953-958, XP002253974 Scheme I, compounds 2b, 5 ---	1,20-27, 30
X	DATABASE CAPLUS 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; retrieved from STN, accession no. AN:1998:348612 Database accession no. DN:129:122614 XP002253978 see RN: 210426-48-5 abstract & MARCHAND, P. ET AL.: PHARMACY AND PHARMACOLOGY COMMUNICATION, vol. 4, no. 4, 1998, pages 211-218, ---	1,3-5, 14,20-26
X	KETCHA, D., M. ET AL: "A Convenient Synthesis of 3-Acylindoles via Friedel-Crafts Acylation of 1-(phenylsulfonyl)indole. A New Route to Pyridocarbazole-5,11-quinones and Elliceptine" THE JOURNAL OF ORGANIC CHEMISTRY, vol. 50, no. 26, 27 December 1985 (1985-12-27), pages 5451-5457, XP002253975 Scheme 2, compound 2h ---	27,30
P,X	SEEBACH, D. ET AL.: "Design and Synthesis of gamma-Dipeptide Derivatives with Submicromolar Affinities for Human Somatostatin Receptors" ANGEW. CHEM. INT. , vol. 42, no. 7, 17 February 2003 (2003-02-17), pages 776-778, XP002253976 compound: 1-mesitylsulfonyl-3-bromomethylindole page 776, right-hand column, line 1,2 --- -/--	27,30

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	PATENT ABSTRACTS OF JAPAN vol. 017, no. 345 (C-1077), 30 June 1993 (1993-06-30) & JP 05 043544 A (NISSHIN FLOUR MILLING CO LTD), 23 February 1993 (1993-02-23) See compound 28, page 333 abstract ---	27,30
X	ZHANG P ET AL: "Regiospecific Bromination of 3-Methylindoles With N-Bromosuccinimide" TETRAHEDRON LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 36, no. 18, 1 May 1995 (1995-05-01), pages 3103-3106, XP004028200 ISSN: 0040-4039 scheme 1, compounds 1a,1c,1e ---	27,30
X	DATABASE CROSSFIRE BEILSTEIN 'Online! Beilstein Institut zur Förderung der Chemischen Wissenschaften, Frankfurt am Main, DE; Database accession no. BRN:6339193 XP002253979 abstract & SYNTH. COMMUN., vol. 23, no. 14, - 1993 pages 2011-2017, ---	27,30
X	DATABASE CROSSFIRE BEILSTEIN 'Online! Beilstein Institut zur Förderung der Chemischen Wissenschaften, Frankfurt am Main, DE; Database accession no. BRN:6149229 XP002253980 abstract & CHEM. SOC. PERKIN TRANS., vol. 13, - 1993 pages 1425-1432, ---	27,30
X	DATABASE CROSSFIRE BEILSTEIN 'Online! Beilstein Institut zur Förderung der Chemischen Wissenschaften, Frankfurt am Main, DE; Database accession no. BRN:1389548 XP002253981 abstract & PHARM. PHARMACOL. COMMUNICATION, vol. 4, no. 4, - 1998 pages 211-218, ---	27,30

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE CROSSFIRE BEILSTEIN 'Online! Beilstein Institut zur Förderung der Chemischen Wissenschaften, Frankfurt am Main, DE; Database accession no. BRN:6339193 XP002253983 abstract & SYNTH. COMMUN., vol. 23, no. 14, - 1993 pages 2011-2017, ---	27,30
X	DATABASE CROSSFIRE BEILSTEIN 'Online! Beilstein Institut zur Förderung der Chemischen Wissenschaften, Frankfurt am Main, DE; Database accession no. BRN:4193743 XP002253984 abstract & TETRAHEDRON LETT., vol. 31, no. 33, - 1990 pages 4697-4698, ---	27,30
X	DATABASE CAPLUS 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; retrieved from STN, accession no. AN:2002:288045 Database accession no. DN:137:310781 XP002253985 see compound RN:471294-27-6 abstract & JOURNAL OF THE ARKANSAS ACADEMY OF SCIENCE, vol. 54, - 2000 pages 33-37, ---	27,30
X	DATABASE CAPLUS 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; retrieved from STN, accession no. AN:2003:475519 Database accession no. DN:139:6769 XP002253986 abstract & CN 1 345 724 A 24 April 2002 (2002-04-24) ---	27,30
X	DATABASE CROSSFIRE BEILSTEIN 'Online! Beilstein Institut zur Förderung der Chemischen Wissenschaften, Frankfurt am Main, DE; Database accession no. BRN:7538920 XP002253987 abstract & J. CHEM. SOC. CHEM. COMMUN., vol. 12, - 1996 pages 1417-1418, ---	28,29
	-/--	

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE CROSSFIRE BEILSTEIN 'Online! Beilstein Institut zur Förderung der Chemischen Wissenschaften, Frankfurt am Main, DE; Database accession no. BRN:8491943 XP002253988 abstract & SYNTHESIS, vol. 4, - 2000 pages 549-556, ---</p>	28,29
X	<p>DATABASE CROSSFIRE BEILSTEIN 'Online! Beilstein Institut zur Förderung der Chemischen Wissenschaften, Frankfurt am Main, DE; Database accession no. BRN:4488731 XP002253989 abstract & CAN. J. CHEM., vol. 67, - 1989 pages 1071-1076, ---</p>	28,29
X	<p>MALLERON J-L ET AL: "NEW INDOLE DERIVATIVES AS POTENT AND SELECTIVE SEROTONIN UPTAKE INHIBITORS" JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY. WASHINGTON, US, vol. 36, no. 9, 1993, pages 1194-1202, XP000195950 ISSN: 0022-2623 example 21; table 2 ---</p>	31,32
X	<p>DATABASE CROSSFIRE BEILSTEIN 'Online! Beilstein Institut zur Förderung der Chemischen Wissenschaften, Frankfurt am Main, DE; Database accession no. BRN: 1592954 XP002253990 abstract & J. MED. CHEM., vol. 9, - 1966 pages 140-142, ---</p>	31,32
X	<p>DATABASE CROSSFIRE BEILSTEIN 'Online! Beilstein Institut zur Förderung der Chemischen Wissenschaften, Frankfurt am Main, DE; Database accession no. BRN: 885083 XP002253991 abstract & SYN. LETT., vol. 10, - 1998 pages 1123-1125, ---</p>	31,32

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>MUTULIS, F. ET AL: "Reductive Amination Products Containing Naphthalene and Indole Moieties Bind to Melanocortin Receptors" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, vol. 12, no. 7, - 8 April 2002 (2002-04-08) pages 1035-1038, XP002253977 Scheme 1, compound 6c</p> <p>----</p>	31,32
X	<p>GB 1 305 458 A (AGENCE NATIONAL DE VALORISATION DE LA RECHERCHE) 31 January 1973 (1973-01-31) Formula I examples 10,13</p> <p>----</p>	31,32
A	<p>WO 92 13856 A (PFIZER) 20 August 1992 (1992-08-20) page 2, line 1 -page 5, line 27</p> <p>----</p>	1-32
A	<p>WO 96 03400 A (MACOR JOHN EUGENE ;PFIZER (US)) 8 February 1996 (1996-02-08) page 2, line 26 -page 4, line 27</p> <p>----</p>	1-32
A	<p>RUSSELL M G N ET AL: "N-Arylsulfonylindole derivatives as serotonin 5 - HT6 receptor ligands" JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY. WASHINGTON, US, vol. 44, no. 23, 8 November 2001 (2001-11-08), pages 3881-3895, XP002234833 ISSN: 0022-2623 tables 1,4</p> <p>-----</p>	1-32

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 27 (part) -32 (part)

The initial phase of the search revealed a very large number of documents relevant to the issue of novelty of the intermediates of formula (II), (XI) and (IV). So many documents were retrieved that it is impossible to determine which parts of the claim(s) may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT). For these reasons, a meaningful search over the whole breadth of the claims concerning the intermediates is impossible. Consequently, the search for claims 27-32 has been restricted considering the structures of the compounds exemplified in the following manner:

- Formulas (II) and (XI): compounds in which R is SO₂Aryl, R₁, R₃, R₄, R₁₀ are H, A is selected from CH₂, CO, SO₂

- Formula (IV): compounds in which R₁ to R₄ and R₁₀ are H, A is CH₂, CO or SO₂ and the group N(R₁₃)C(R₁₄)(R₁₅)N(R₁₆)(R₁₇) is a piperazine ring eventually substituted by a CH₃ at the free nitrogen.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IN 03/00209

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Although claim(s) 6,8-11,15-18 are directed to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.: 27 (part) -32 (part)
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 02058702	A	01-08-2002	WO 02058702 A1	01-08-2002
WO 0247687	A	20-06-2002	AU 2604802 A WO 0247687 A1	24-06-2002 20-06-2002
JP 2000344744	A	12-12-2000	NONE	
JP 05043544 4	A		NONE	
CN 1345724	A	24-04-2002	NONE	
GB 1305458	A	31-01-1973	FR 2034217 A5 FR 2080854 A6 CH 510017 A DE 2008692 A1	11-12-1970 26-11-1971 15-07-1971 17-09-1970
WO 9213856	A	20-08-1992	AT 135005 T AU 655456 B2 AU 1263792 A CZ 9301656 A3 DE 69208868 D1 DE 69208868 T2 DK 571471 T3 EP 0571471 A1 ES 2084347 T3 FI 933551 A GR 3019778 T3 HU 65766 A2 IE 920442 A1 JP 7121942 B JP 6500122 T MX 9200569 A1 NO 932859 A NZ 241584 A PT 100114 A WO 9213856 A1 ZA 9200969 A	15-03-1996 22-12-1994 07-09-1992 18-05-1994 11-04-1996 17-10-1996 01-04-1996 01-12-1993 01-05-1996 11-08-1993 31-07-1996 28-07-1994 12-08-1992 25-12-1995 06-01-1994 01-08-1992 11-08-1993 22-12-1994 31-05-1993 20-08-1992 11-08-1993
WO 9603400	A	08-02-1996	CA 2194984 A1 EP 0773942 A1 FI 970310 A WO 9603400 A1 JP 3155008 B2 JP 9508137 T US 6255306 B1	08-02-1996 21-05-1997 24-01-1997 08-02-1996 09-04-2001 19-08-1997 03-07-2001